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EXAMINER	
KUDLA, JOSEPH S	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,318	GAMELIN ET AL.	
	Examiner	Art Unit	
	Joseph S. Kudla	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 8-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6 and 8-12* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/7/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Summary from Amendment

1. Applicants' Amendment filed December 3, 2007 is acknowledged. The amended Abstract is acknowledged. The Examiner acknowledges that claims 2 and 7 have been cancelled, leaving claims 1, 3-6 and 8-12 presented to be considered on the merits of the application.

Applicants' arguments have been fully considered. Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

2. The Information Disclosure Sheet (IDS) correspondence submitted by Applicant on November 7, 2007 is acknowledged and has been reviewed to the extent each is a proper citation and has been supplied.

Specification

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.

(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) The Names Of The Parties To A Joint Research Agreement: See 37 CFR 1.71(g).

(e) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent

application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.

(f) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(g) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(h) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(i) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an

understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(j) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(k) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

(l) Sequence Listing, See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

3. The specification of a utility application should include the above sections in order. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading. Specifically, none of the section headings or a disclosure of joint research agreements or a cross-reference to related applications are present.

Appropriate action is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 3-6, 8-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to provide adequate written description for the describing the use of both an injectable and an oral form of calcium. Nowhere in Applicants' instant specification is there any written description showing examples, or incorporated by reference as prior art, calcium used in both dosage forms simultaneously, sequentially or separately. Because it is readily known in the prior art that injectable solutions of calcium and magnesium are administered parenterally, simultaneously or after injection of oxaliplatin to treat neurotoxicity (see 35 USC 102 rejection as being clearly anticipated by Laine-Cessac et al. in office action mailed 8/28/2007). Applicant's inventive concept appears to be the administration of an oral form of calcium at the time of the injections of magnesium and calcium, before or for a period thereafter.

Accordingly, it is imperative that an adequate written description is provided in the form of written examples, scholarly discussion or prior art incorporated by reference. Applicants have provided none of these exemplifications; therefore the instant specification lacks adequate written description for the administration of calcium in an oral and a parenteral dosage at any time.

5. Claims 1, 3-6, 8-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the prevention or treatment of neurotoxicity by administering a product that releases oxalate during its metabolism with calcium and magnesium; where the magnesium is dosed in a parenteral dosage form and the calcium is dosed in both an oral and a parenteral dosage form at a time prior to, after, during or in any sequence.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims without undue experimentation to treat neurotoxicity.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)*. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without

undue experimentation.

These factors include:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

The breadth of the instant claims is broad in scope for the administration schedule of the treatment regimen. Applicant has not provided sufficient evidence to support a claim set drawn to the prevention or treatment of neurotoxicity by administering a product that releases oxalate during its metabolism with calcium and magnesium, where the magnesium is dosed in a parenteral dosage form and the calcium is dosed in both an oral and a parenteral dosage form at a time prior to, after, during or in any sequence. In addition, prevention of most disorders/conditions/diseases

treated by pharmaceutical means remains largely an elusive goal. The breadth of the claims exacerbates the complex nature of the subject matter to which the present claims are directed.

The nature of the invention

The instant claim set outlines two inventions (a composition and a method) wherein prevention or treatment of neurotoxicity by administering a product that releases oxalate during its metabolism with calcium and magnesium, where the magnesium is dosed as a parenteral dosage form and the calcium is dosed in both an oral and a parenteral dosage form at a time prior to, after, during or in any sequence. The instant claims disclose the calcium and magnesium can exist in various salts and the daily dosages to be administered.

The state of the prior art

Prior art in the field shows injectable solutions of calcium and magnesium are administered parenterally, simultaneously or after injection of oxaliplatin to treat neurotoxicity (Laine-Cessac et al.). However, the prior art is silent with respect to a discrete oral calcium dosage administered prior, during or after the regimen outlined in the prior art for the benefit of either acute or chronic neurotoxicity.

The level of predictability in the art

The instant claimed invention is highly unpredictable. Due to the general unpredictability in the pharmaceutical art and the lack of prior art showing the effects of an oral calcium dosage form on acute and chronic neurotoxicity, Applicant would need to show evidence that the oral dosage would have the desired physiological response through examples or scholarly discussion showing the nexus between what is commonly known in the art and that which Applicant asserts is his invention. In this particular case, the oral calcium dosage, in the salt forms outlined by Applicant in the instant specification, is required to be assessed for physiological activity by *in vivo* screening to determine if the oral dosage exhibits the desired pharmacological activity of treating or preventing neurotoxicity. Of the three studies disclosed by applicant in the instant specification on pages 9-11, none of the subjects were given an oral dose of any calcium salt at any time. Furthermore, all three studies only show that the regular infusion of calcium and magnesium are required to alleviate the onset of neurotoxicity which is readily known in the art. No studies were conducted with oral calcium and no drug treatment regimens comprising administering compositions of oxaliplatin, injectable magnesium and calcium and an oral form of calcium have been disclosed. Because the prior art and the discussion by Applicant are silent to the feasibility of an oral formulation of calcium given at any time to treat neurotoxicity for any product that releases oxalate during its metabolism, one of ordinary skill in the art would have considered the invention speculative. Applicant provides no correlation of the administration of an oral formulation of calcium given at any time to treat neurotoxicity for any product that releases oxalate during its metabolism. Therefore, one cannot reasonably predict the

ability of the composition to elicit *any* pharmacological response, because the results were neither exemplified in Applicants' specification nor shown in the prior art. Parameters assessed in the study are not adequate to support *any* of Applicants' instant claims and one cannot predict efficacy for an oral formulation of calcium given at any time to treat neurotoxicity for any product that releases oxalate during its metabolism.

Applicant is reminded of the decision *Genentech Inc. vs. NovaNordisk* which states, " [A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

In addition, "to prevent", as defined by Merriam-Webster Dictionary is to keep from happening or existing, which implies taking advance measures against something possible or probable. Furthermore, the definition of "to prevent" and the "act of preventing" embraces the complete 100% inhibition. Thus, the burden of enablement in the assertion of this claim is much higher than would be the case of enabling the treatment of the condition and is not achieved. Nowhere in the prior art or instant application has the oral calcium formulation in the instant claim set been enabled to prevent or treat neurotoxicity.

The existence of these obstacles establishes that the contemporary knowledge in the art would have prevented one of ordinary skill in the art from accepting any therapeutic regimen for the treatment of neurotoxicity with the Applicants' proposed drug regimen on its face. *In re Fisher, 427 F. 2d, 833, 166 USPQ 18 (CCPA 1970),*

indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Hence, one of skill in the art is unable to fully predict the ability of an oral formulation of calcium given at any time to prevent or treat neurotoxicity for any product that releases oxalate during its metabolism.

The amount of direction provided by the inventor and the existence of working examples

The instant specification does not provide adequate guidance, which would allow the skilled artisan to extrapolate from the disclosure and examples provided, to practice the claimed methods commensurate in the scope with the instant claims. Applicant provides *no* guidance using an oral formulation of calcium given at any time as specified in instant claims 1 and 6, *no* guidance demonstrating the ability of an oral formulation of calcium given at any time to prevent or treat neurotoxicity and *no* guidance demonstrating the treatment of neurotoxicity with an oral calcium formulation during the oxaliplatin drug regimen with infusions of magnesium and calcium within adequate control/study measures. Adequate enablement requires more than a mere statement that a compound treats a given condition.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation (*In re Wright, 999 F. 2d 1557, 1562; 27 USPQ 2d 1510, 1514 (Fed. Cir. 1993)*). The specification lacks sufficient disclosure

to support applicant's claims of the ability of an oral formulation of calcium given at any time to prevent or treat neurotoxicity for any product that releases oxalate during its metabolism. There is not seen sufficient working examples or data from references in the prior art providing a nexus between that which applicant asserts is supporting a method of treating or preventing neurotoxicity with an oral formulation of calcium and the amount of disclosure Applicant has actually provided.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Based on the unpredictable nature of the invention, the state of the prior art and the breadth of the claims, one skilled in the art could not have practiced the claimed invention without undue experimentation. The essential element towards the validation of a therapeutic modality capable of performing the mechanism of action is the ability to test the compound or composition within *specific parameters* in advance of administration of a compound and, while maintaining experimental control, link those results with sampling time points. Once it can be documented that the compound/composition of interest elicits a desired pharmacological response within experimental controls, the compound, for the sake of this forum, could generally be assumed to have that pharmacological activity.

Based on the unpredictable nature of the invention, the state of the prior art and the extreme breadth of the claims, one skilled in the art could not have practiced the claimed invention without undue experimentation.

6. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase, "the concentrations being expressed as calcium ion," in lines 6-7 of instant claim 5 is confusing due to the preceding statement referring to the calcium and magnesium concentrations. It is believed applicant meant "the concentrations being expressed in calcium and magnesium ions, respectively." Therefore, if Applicant had meant to claim the concentrations of the respective ions, this leaves the Examiner to question the meaning of Applicants' claimed invention, thereby rendering the subject matter of the instant claim unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 3-6 and 8-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laine-Cessac et al. ("Acute Oxaliplatin Neurotoxicity Dramatically Improved with Intravenous Calcium and Magnesium Salts," Therapie, Vol. 53 page 183, 1998), in view of Chazard (US Patent Publication US 2002/0045632).

Laine-Cessac et al. teaches that the anticancer agent (line 5) oxaliplatin–induced neurotoxicity (1st sentence) can be dramatically improved after simultaneous (patient F/49 in table- given 4 minutes after the start of the 2-hour infusion of oxaliplatin) or post-injection (patient F/59 in table—given 15 minutes after the end of the infusion) administration of calcium and magnesium. Patients were intravenously administered a mixture of calcium gluconate and magnesium sulfate (1st sentence below table).

Laine-Cessac et al. does not teach the use of an oral calcium formulation nor the administration dosages or schedules.

Chazard teaches the use of an oral formulation of calcium folinate and an intravenous administration oxaliplatin (paragraph 36) to treat tumors (Abstract). Chazard teaches the calcium folinate is to be administered for 1-14 days (paragraph 36). Chazard also teaches an example (Example 2, pages 3 and 4) calculating the maximal tolerated dose of oxaliplatin with calcium folinate (page 3, paragraph 33). One of the

parameters for selection into the study was that the subjects exhibit "no evidence of peripheral neuropathy" (page 3, paragraph 34). Chazard teaches that 19 subjects (page 4, paragraph 38) were treated with up to 130 mg/m^2 of oxaliplatin while being treated with 90 mg/day of calcium folinate (page 3, table after paragraph 5) without experiencing dose limiting toxicity (page 4, paragraph 38).

It would have been obvious to one of ordinary skill in the art, in view of the teachings of Laine-Cessac et al., drawn to a parenteral composition comprising a parenteral drug regimen of oxaliplatin and magnesium and calcium salts in the treatment of adenocarcinoma, and Chazard, drawn to an oral formulation of calcium folinate and an intravenous administration oxaliplatin to treat tumors, a preparation of all of the elements of both formulations would similarly be useful in treating tumors and alleviating neuropathy. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be *prima facie* obvious.). Therefore, combining the teachings of Laine-Cessac et al. and Chazard would have resulted in a drug regimen for the treatment of cancer that contained an oral calcium dosage, a parenteral dosage of calcium and magnesium and an active ingredient which releases oxalate during its metabolism (e.g., oxaliplatin).

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.). Therefore, no more than routine experimentation would have been necessary to one of ordinary skill in the art to arrive at both the administration dosages, a dosage schedule (e.g., prior, after, during, sequential, separately, etc.) recited in instant claims 1, 5, 6 and 9-12 and an optimal oral formulation of a calcium salt that would be easily assimilated in the body, as in instant claim 4.

Therefore, the teachings of Laine-Cessac et al., in view of Chazard, render the claimed invention obvious.

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph S. Kudla whose telephone number is (571) 270-3288. The examiner can normally be reached on 9am - 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JK

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER

2/2/08